

**REMARKS**

The Applicants appreciate the Examiner's thorough examination of the subject application. Claims 1, 11, 15, 18, 19, and 26 have been amended. Claims 3 and 4 stand canceled. Claims 15-25 are withdrawn. Accordingly, claims 1, 2, and 5-26 are pending in the application. Applicants request reconsideration of the subject application based on the following remarks. No new matter has been introduced by the instant amendments.

Amendment of any claim herein is not to be construed as acquiescence to any of the rejections/objections set forth in the instant Office Action, and was done solely to expedite prosecution of the application. Applicants make these amendments without prejudice to pursuing the original subject matter of this application in a later filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject matter.

Upon allowance of the claims directed to newly reformulated heteroaryl pyridine-pyrazine compounds and pyrimidine-pyrazine compounds, Applicants respectfully request rejoinder of the subject matter excised by the Examiner's oral restriction requirement of claims 15-25, e.g., the rejoinder of claims directed to methods of use, pharmaceutical compositions, and packages.

As an initial matter, Applicants thank the Examiner for the courtesy of a number of telephonic discussions from mid-October to the beginning of November, 2005. During the course of the discussions, the Examiner rejected claims 1 and 18 under 35 U.S.C. §112, second paragraph. Claims 15, 16, and 19 were rejected under 35 U.S.C. §112, first paragraph, allegedly due to lack of enablement.

Claim 1 has been amended to remove the redundant recitation of "halogen" at R<sub>7</sub>, and to more clearly delineate the instant invention regarding the 2,2,2-trifluoro-1-hydroxyethyl group at R<sub>7</sub>. Claim 1 has been further amended to remove certain definitions at variables K, R<sub>7</sub>, and R<sub>8</sub>. Specifically, K has been amended to replace "CR<sub>6</sub>" with "CH". R<sub>7</sub> has been amended to remove the recitation of "mono- and di-(C<sub>1-2</sub>alkyl)aminoC<sub>1-4</sub>alkyl." R<sub>8</sub> has been amended to remove the

recitation of “hydrogen.” As a consequence of the instant amendments, claims 11 and 26 have been amended to remove compounds not in accordance with the amended definitions of K, R<sub>7</sub>, and R<sub>8</sub>. The rejection is thus overcome and withdrawal of the rejection is requested.

Claim 18 has been amended to overcome the allegation that “tablet” and “pill” are synonymous. Claims 15 and 19 are amended to remove the allegedly indefinite term “stress.” The rejections are thus overcome and withdrawal of the rejections is requested.

Claim 16 has been rejected, allegedly due to lack of enablement of the instant invention for a method for treating irritable bowel syndrome (IBS) or Crohn’s disease. Applicants submit herewith the following three journal articles: Y. Sagami et al. Gut (2004), 53, 958; Y. Tache, Gut (2004), 53, 919; and V. Martinez et al. J. Physiol (2004), 556.1, 221. Sagami indicates that certain CRF receptor antagonists reduced the ordinate scale of abdominal pain and anxiety evoked by ES in IBS patients (see page 958 abstract). Tache confirms this conclusion at page 920, wherein the “intravenous injection of certain CRF receptor antagonists blunts the exaggerated motility response in the sigmoid colon to electrical stimulation in IBS patients,” and that the “CRF antagonist reduces significantly abdominal pain and anxiety.” Additionally, Martinez notes that agonists and antagonists for CRF receptors provide for gastric emptying and stimulating distal colonic propulsion and defecation in mice (page 232).

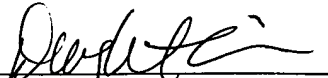
IBS and Crohn’s disease are related in that both are disorders of the gastrointestinal/digestive tract. Thus, the Sagami and Tache articles provide support for the use of CRF receptor antagonists to treat pain associated with IBS and Crohn’s disease, and Martinez indicates the use of CRF receptor agonists and antagonists to increase gastric emptying. Applicants therefore indicate that the compounds of the instant invention are enabled to treat IBS and Crohn’s disease.

Thus, for at least the reasons recited *supra*, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be allowable, the Examiner is requested to telephone Applicant's undersigned representative at the number below. Applicant thanks the Examiner in advance for this courtesy.

Although it is not believed that any additional fees are needed to consider this submission, the Examiner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

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Respectfully submitted,

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